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WO 2003/087368 A3

(54) Title: MEANS AND METHODS FOR THE SPECIFIC MODULATION OF TARGET GENES IN THE CNS AND THE EYE AND METHODS FOR THEIR IDENTIFICATION

(57) Abstract: Provided are methods for the treatment of disorders of the central nervous system (CNS) and the eye. In particular, use of compositions comprising a compound capable of modulating a target gene or gene product is described for the preparation of a pharmaceutical composition for the treatment of disorders of the CNS and/or the eye, wherein the composition is designed to be administered outside the blood-CNS and the blood-retina barriers. Furthermore, methods are provided for identifying and obtaining nucleic acid molecules encoding polypeptides involved in CNS disorders or of the eye, methods for diagnosing said disorders as well as transgenic animal deficient in the expression of target genes identified in accordance with the described method. In addition, methods of identifying and isolating drugs that are particularly useful for the treatment of disorders related to the CNS and/or the eye are disclosed.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/04003

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/11 A61K48/00 A61K31/713 A61K9/08 C12Q1/68
C12N15/12 C07K14/47 C07K16/18 G01N33/50 G01N33/68
A01K67/027

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N A61K C12Q C07K G01N A01K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
20 January 2004	06 FEB 2004

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Macchia, G

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 1 and 3-23 are directed to a method of treatment of the human/animal body, the search, has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [X] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

1-23, all partially insofar as they refer to subject-matter related to the inventions 1, 6 and 7.

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[X] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1, 2, 9, 11-18, 20-22 all partially

A method for the treatment of a disorder of the central nervous system (CNS) comprising administering to a subject a composition comprising a compound capable of modulating a target gene or gene product in a therapeutically effective amount, wherein said composition is administered outside the blood-brain barrier.
Use of a compound capable of modulating a target gene or gene product for the preparation of a pharmaceutical composition for the treatment of a disorder of the central nervous system (CNS), wherein said composition is designed to be applied outside the blood-brain barrier.
Said method or use wherein said compound is an inhibitor/antagonist of said target gene or gene product, said inhibitor/antagonist being derived from a nucleic acid molecule (ribozyme, antisense).
Methods or uses related thereto.

2. Claims: 1, 2, 9, 11-18, 20-22 all partially, if and where applicable

A method for the treatment of a disorder of the central nervous system (CNS) comprising administering to a subject a composition comprising a compound capable of modulating a target gene or gene product in a therapeutically effective amount, wherein said composition is administered outside the blood-brain barrier.
Use of a compound capable of modulating a target gene or gene product for the preparation of a pharmaceutical composition for the treatment of a disorder of the central nervous system (CNS), wherein said composition is designed to be applied outside the blood-brain barrier.
Said method or use wherein said compound is an inhibitor/antagonist of said target gene or gene product, said inhibitor/antagonist being derived from a nucleic acid molecule (sense nucleic acid molecule).
Methods or uses related thereto.

3. Claims: 1, 2, 9, 11, 20-22 all partially

A method for the treatment of a disorder of the central nervous system (CNS) comprising administering to a subject a composition comprising a compound capable of modulating a target gene or gene product in a therapeutically effective amount, wherein said composition is administered outside the blood-brain barrier.
Use of a compound capable of modulating a target gene or gene product for the preparation of a pharmaceutical

composition for the treatment of a disorder of the central nervous system (CNS), wherein said composition is designed to be applied outside the blood-brain barrier.
Said method or use wherein said compound is an inhibitor/antagonist of said target gene or gene product, said inhibitor/antagonist being derived from a polypeptide.
Methods or uses related thereto.

4. Claims: 1, 2, 9-11, 20-22 all partially

A method for the treatment of a disorder of the central nervous system (CNS) comprising administering to a subject a composition comprising a compound capable of modulating a target gene or gene product in a therapeutically effective amount, wherein said composition is administered outside the blood-brain barrier.
Use of a compound capable of modulating a target gene or gene product for the preparation of a pharmaceutical composition for the treatment of a disorder of the central nervous system (CNS), wherein said composition is designed to be applied outside the blood-brain barrier.
Said method or use wherein said compound is an inhibitor/antagonist of said target gene or gene product, said inhibitor/antagonist being derived from an antibody.
Methods or uses related thereto.

5. Claims: 1, 2, 9, 11, 20-22 all partially

A method for the treatment of a disorder of the central nervous system (CNS) comprising administering to a subject a composition comprising a compound capable of modulating a target gene or gene product in a therapeutically effective amount, wherein said composition is administered outside the blood-brain barrier.
Use of a compound capable of modulating a target gene or gene product for the preparation of a pharmaceutical composition for the treatment of a disorder of the central nervous system (CNS), wherein said composition is designed to be applied outside the blood-brain barrier.
Said method or use wherein said compound is an inhibitor/antagonist of said target gene or gene product, said inhibitor/antagonist being derived from a ligand binding molecule of said gene or gene product.
Methods or uses related thereto.

6. Claims: 1-23 all partially

A method for the treatment of a disorder of the eye comprising administering to a subject a composition comprising a compound caable of modulating a target gene or gene product in a therapeutically effective amount, wherein said composition is administered outside the blood-retina

barrier.
Use of a compound capable of modulating a target gene or gene product for the preparation of a pharmaceutical composition for the treatment of a disorder of the eye, wherein said composition is designed to be applied outside the blood-retina barrier.
Said method or use wherein said compound is an inhibitor/antagonist of said target gene or gene product, said inhibitor/antagonist being derived from a nucleic acid molecule (ribozyme, antisense).
Methods or uses related thereto.

7. Claims: 1-23 all partially, if and where applicable

A method for the treatment of a disorder of the eye comprising administering to a subject a composition comprising a compound caable of modulating a target gene or gene product in a therapeutically effective amount, wherein said composition is administered outside the blood-retina barrier.
Use of a compound capable of modulating a target gene or gene product for the preparation of a pharmaceutical composition for the treatment of a disorder of the eye, wherein said composition is designed to be applied outside the blood-retina barrier.
Said method or use wherein said compound is an inhibitor/antagonist of said target gene or gene product, said inhibitor/antagonist being derived from a nucleic acid molecule (sense nucleic acid molecule).
Methods or uses related thereto.

8. Claims: 1-11, 19-23 all partially

A method for the treatment of a disorder of the eye comprising administering to a subject a composition comprising a compound caable of modulating a target gene or gene product in a therapeutically effective amount, wherein said composition is administered outside the blood-retina barrier.
Use of a compound capable of modulating a target gene or gene product for the preparation of a pharmaceutical composition for the treatment of a disorder of the eye, wherein said composition is designed to be applied outside the blood-retina barrier.
Said method or use wherein said compound is an inhibitor/antagonist of said target gene or gene product, said inhibitor/antagonist being derived from a polypeptide.
Methods or uses related thereto.

9. Claims: 1-11, 19-23 all partially

A method for the treatment of a disorder of the eye

comprising administering to a subject a composition comprising a compound caable of modulating a target gene or gene product in a therapeutically effective amount, wherein said composition is administered outside the blood-retina barrier.
Use of a compound capable of modulating a target gene or gene product for the preparation of a pharmaceutical composition for the treatment of a disorder of the eye, wherein said composition is designed to be applied outside the blood-retina barrier.
Said method or use wherein said compound is an inhibitor/antagonist of said target gene or gene product, said inhibitor/antagonist being derived from an antibody.
Methods or uses related thereto.

10. Claims: 1-11, 19-23 all partially

A method for the treatment of a disorder of the eye comprising administering to a subject a composition comprising a compound caable of modulating a target gene or gene product in a therapeutically effective amount, wherein said composition is administered outside the blood-retina barrier.
Use of a compound capable of modulating a target gene or gene product for the preparation of a pharmaceutical composition for the treatment of a disorder of the eye, wherein said composition is designed to be applied outside the blood-retina barrier.
Said method or use wherein said compound is an inhibitor/antagonist of said target gene or gene product, said inhibitor/antagonist being derived from a ligand binding molecule of said gene or gene product.
Methods or uses related thereto.

11. Claims: 24-90 all totally

A method as defined in claim 24.
Methods, products, compositions, uses, kits, chips related thereto.

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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INTERNATIONAL SEARCH REPORT

International Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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